and growth retardation, rises with increasing doses of inhaled corticosteroids. Therefore, the need for high doses of inhaled corticosteroids in a patient should be constantly reassessed so as to administer the lowest effective dose. In one study, when the same microgram doses of BDP, TAA, and FL were administered, equivalent suppression of 24-hour urinary-free cortisol excretion was observed. FP had greater adrenal suppression than BUD, however, at equivalent microgram doses even when accompanied by a mouth-washing procedure to prevent oral bioavailability.

Overall, selected inhaled corticosteroids (such as BDP) have been associated with remarkably few side effects at doses up to 400 µg per day in children and up to 800 µg per day in adults. Even at higher doses—up to 2000 µg per day—relatively few adverse events have been reported. In conclusion, the small risk associated with inhaled corticosteroids must be balanced against the far greater dangers of failing to control chronic asthma.

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Intravenous Immune Globulin in Neuromuscular Disorders

Intravenous immune globulin (IVIG) is a polyvalent immunoglobulin that contains more than 90% monomeric IgG with small amounts of other immunoglobulins, such as IgA, IgM, and possibly IgE. It is prepared from plasma derived from a large pool of volunteer donors. (The donors are well screened for human immunodeficiency virus [HIV], human T-cell lymphotropic virus, and the hepatitis A, B, and C viruses. In addition, HIV and hepatitis B virus are inactivated by a fractionation process, and the plasma is treated with solvents, detergents, or enzymes and incubated at low pH to inactivate hepatitis C and other viruses.)

IVIG is primarily used as a replacement therapy for patients with antibody deficiencies. The successful use of high doses of IVIG to treat children with idiopathic thrombocytopenic purpura led to high doses (approximately a total initial dose of 2 g/kg body weight over five consecutive days) being used in a large number of autoimmune disorders, including several neuromuscular disorders. In some, such as Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy, and dermatomyositis, the results of controlled clinical trials have demonstrated definite beneficial effects. In fact, a number of controlled studies, including multinational and multicenter studies, of Guillain-Barré syndrome—a monophasic acute demyelinating polyneuropathy characterized by severe weakness or paralysis of limbs and respiratory muscles—have demonstrated that high-dose IVIG therapy is at least as effective as plasmapheresis or combination of IVIG and plasmapheresis. The efficacy of IVIG in other disorders is either anecdotal or not fully substantiated by controlled studies. The beneficial effect of the combination of intravenous methylprednisone plus IVIG over IVIG alone remains to be determined.

Taking into consideration cost, safety, convenience, and practicality, IVIG is preferred for small children or patients with poor venous access, patients with severe autonomic dysfunction or compromised hemodynamics, and patients in hospitals in which plasmapheresis is either not available or not routinely performed.

Unlike Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), characterized by the slow onset of weakness, areflexia, and impaired sensation, requires long-term therapy to maintain improvement. The treatments for CIDP are steroids, high-dose IVIG, and plasmapheresis. The response to steroids is sometimes slow, and prolonged therapy increases the risk for severe side effects. Controlled and randomized studies have demonstrated that high-dose IVIG and plasmapheresis are equally effective in improving muscle strength, neuropathic symptoms, and amplitude of evoked muscle-action potentials. At this stage, it is unclear what dose should be used for maintenance therapy, although a monthly administration of 1 g/kg body weight has been recommended.

Multifocal motor neuropathy (MFMN) is a disorder of slow onset of weakness and muscular atrophy with areflexia and without sensory loss. It is characterized by conduction block of the motor axons and by the presence of GM1 ganglioside antibodies. IVIG is the treatment of choice for MFMN. IVIG therapy is associated with diminution of symptoms and resolution of electrophysiological conduction block, although GM1 antibody titers may be unaffected. If the efficacy of IVIG therapy diminishes after several months of treatment, the coadministration of intravenous cyclophosphamide may be indicated.

Dermatomyositis is a myopathy characterized by weakness of proximal muscles, violaceous rash on the face and extremities, and deposits of immune complexes in the capillaries. Double-blind and controlled studies have demonstrated that high-dose IVIG induces clinical improvement that is associated with inhibition of the deposition of components of complement activation and downregulation of intercellular adhesion molecule-1 and major histocompatibility complex (MHC) class I. Since steroids are the treatment of choice, IVIG is indicated for steroid-resistant patients or for patients in whom steroids are contraindicated.

The side effects of IVIG treatment occur in less than 10% of cases, and are usually minor: mild-to-moderate headache, chills, myalgia, chest discomfort, fever,

fatigue, and nausea. Most of the side effects can be prevented or treated by administration of nonsteroidal anti-inflammatory agents and by slowing the rate of IVIG infusion. Aseptic meningitis occurs in 10% of cases, responds to strong analgesia, and subsides in 24 to 48 hours. Other rare adverse reactions include skin rash, anaphylaxis, and renal tubular necrosis.

The mechanisms by which IVIG exerts its beneficial effects in neuromuscular disorders are not clearly understood, but various immunomodulatory effects have been proposed. IVIG contains a variety of anti-idiotypic antibodies that bind to and neutralize pathogenic autoantibodies, thus preventing their interaction with self-antigens. Along with IgG, molecules in IVIG that have immunomodulatory effects in neuromuscular disorders include antibodies to various cytokines and T cell receptors and soluble CD4, CD8, and MHC class II antigens.

Determination of the optimal dose, frequency, duration, and the mechanisms of action of IVIG in various neuromuscular disorders will continue to challenge scientists. Meanwhile, because IVIG is expensive, the clinician should be judicious in the use of IVIG as a therapeutic agent in neuromuscular disorders.

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